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Table 8. Advantages and Disadvantages of Different Nucleoside or Nucleotide Analogue Reverse Transcriptase Inhibitor (NRTI, NtRTI) Combinations for Use in Highly Active Antiretroviral Combination Regimens

| | Advantages | Disadvantages |
|--|--|---|
| General Issues | | |
| NRTI/NtRTI-Based Regimens | NRTI Class Advantages: <ul style="list-style-type: none"> Minimal drug-drug interactions Protease inhibitor and NNRTI-sparing Only limited cross resistance among NRTIs Easier to use and adhere to than protease inhibitor-based regimens One combination is coformulated as single pill for older/larger patients (ZDV/3TC/ABC, Trizivir); low pill burden | NRTI Class Disadvantages: <ul style="list-style-type: none"> Rare but serious and potentially life-threatening cases of lactic acidosis and hepatic steatosis with all NRTIs/NtRTI ZDV/3TC/ABC (Trizivir) has inferior virologic response compared to efavirenz-based regimens or to indinavir-based regimens in adults Use of ZDV/3TC/ABC (Trizivir) coformulation has potential for ABC hypersensitivity reaction |
| Strongly Recommended Combinations | | |
| ZDV plus 3TC | <ul style="list-style-type: none"> Extensive pediatric experience Coformulated as single pill for older/larger patients Palatable liquid formulations Can give with food | <ul style="list-style-type: none"> Bone marrow suppression with ZDV Single mutation confers 3TC resistance |
| ZDV plus ddI | <ul style="list-style-type: none"> Extensive pediatric experience Videx EC may allow once daily dosing of ddI in older children able to swallow pills and who can receive adult dosing | <ul style="list-style-type: none"> Bone marrow suppression with ZDV Pancreatitis, neurotoxicity with ddI ddI liquid formulation less palatable than 3TC liquid formulation Food effect (ddI needs to be taken 1 hour before or 2 hours after food) |
| d4T plus 3TC | <ul style="list-style-type: none"> Moderate pediatric experience Palatable liquid formulations Can give with food Zerit XR may allow once daily dosing of d4T in older children able to swallow pills and who can receive adult dosing | <ul style="list-style-type: none"> d4T associated with higher incidence of hyperlactatemia/ lactic acidosis, lipodystrophy, peripheral neuropathy, hyperlipidemia Single mutation confers 3TC resistance |
| Alternative Combinations | | |
| ABC plus ZDV | <ul style="list-style-type: none"> Palatable liquid formulations Can give with food | <ul style="list-style-type: none"> Potential for ABC hypersensitivity reaction Bone marrow suppression with ZDV |
| ABC plus 3TC | <ul style="list-style-type: none"> Palatable liquid formulations Can give with food | <ul style="list-style-type: none"> Potential for ABC hypersensitivity reaction Single mutation confers 3TC resistance |
| ddI plus 3TC | <ul style="list-style-type: none"> Videx EC may allow once daily dosing of ddI in older children able to swallow pills and who can receive adult dosing | <ul style="list-style-type: none"> Food effect (ddI needs to be taken 1 hour before or 2 hours after food) Pancreatitis, neurotoxicity with ddI, potentially additive with 3TC Single mutation confers 3TC resistance |

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Table 8. Advantages and Disadvantages of Different Nucleoside or Nucleotide Analogue Reverse Transcriptase Inhibitor (NRTI, NtRTI) Combinations for Use in Highly Active Antiretroviral Combination Regimens

| NRTI (cont) | Advantages | Disadvantages |
|---|--|---|
| <i>Use in Special Circumstances</i> | | |
| d4T plus ddI | <ul style="list-style-type: none"> • Can give with food • Videx EC may allow once daily dosing of ddI in older children able to swallow pills and who can receive adult dosing • Zerit XR may allow once daily dosing of d4T in older children able to swallow pills and who can receive adult dosing | <ul style="list-style-type: none"> • d4T associated with higher incidence of hyperlactatemia/ lactic acidosis, lipoatrophy, peripheral neuropathy, hyperlipidemia than other NRTIs • Potential synergistic toxicity (neurotoxicity, lactic acidosis, hepatic steatosis) of the combination • Food effect (ddI needs to be taken 1 hour before or 2 hours after food) |
| ZDV plus ddC | <ul style="list-style-type: none"> • Can give with food | <ul style="list-style-type: none"> • No liquid formulation ddC • ddC less potent NRTI than other NRTIs • Bone marrow suppression with ZDV • Severe peripheral neuropathy from ddC |
| <i>Insufficient Data to Make Recommendation</i> | | |
| Tenofovir | <ul style="list-style-type: none"> • Resistance slow to develop • Once daily dosing for tenofovir (adults) • Less mitochondrial toxicity than NRTIs • Can give with food | <ul style="list-style-type: none"> • No data on pediatric dosing or safety • Potential bone and renal toxicity • ddI concentrations are increased when given with tenofovir, potential for increased toxicity of ddI |
| FTC | <ul style="list-style-type: none"> • Once daily dosing (adults) • Can give with food | <ul style="list-style-type: none"> • No data on pediatric dosing or safety • No liquid formulation |
| <i>Not Recommended</i> | | |
| ZDV plus d4T | | <ul style="list-style-type: none"> • Pharmacologic and antiviral antagonism |
| ddC plus d4T | | <ul style="list-style-type: none"> • Potentially synergistic neurotoxicity • No liquid formulation ddC |
| ddC plus ddI | | <ul style="list-style-type: none"> • Potentially synergistic neurotoxicity • No liquid formulation ddC |
| ddC plus 3TC | | <ul style="list-style-type: none"> • Potentially synergistic neurotoxicity • No liquid formulation ddC |

NRTI: Nucleoside analogue reverse transcriptase inhibitor

NtRTI: Nucleotide analogue reverse transcriptase inhibitor

ABC: Abacavir

ddC: Zalcitabine

ddI: Didanosine

d4T: Stavudine

FTC: Emtricitabine

3TC: Lamivudine

ZDV: Zidovudine